Non-AIDS defining cancer

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Objectives

• Epidemiology of non-AIDS defining cancers (NADC)
• NADC risk factors
• Identify specific NADC that disproportionately affect the HIV+ population
• General diagnosis and treatment of specific NADC
• NADC screening guidelines, if available
Which of the following are the AIDS-defining cancers?

A. Lung cancer, colon cancer, breast cancer
B. Prostate cancer, non-Hodgkin lymphoma, pancreatic cancer
C. Myeloblastic leukemia, invasive head and neck cancer, Kaposi sarcoma
D. Kaposi sarcoma, non-Hodgkin lymphoma, invasive cervical cancer
• The AIDS-defining cancers (ADC)
  – Kaposi Sarcoma
  – Non-Hodgkin Lymphoma
  – Invasive Cervical Cancer

  – Opportunistic diseases!
  – Highly associated with immunosuppression
Non-AIDS defining cancers

- These include any cancer that isn’t ADC, which may (or may not) disproportionately affect HIV+ individuals.
- The association with immunosuppression depends on the unique cancer type, and is more complicated.
Non-AIDS defining cancer

- Cancers that disproportionately affect the HIV-infected population
  - Hodgkin lymphoma (HL)
  - Hepatocellular carcinoma
  - Lung cancer
  - Head and neck squamous cell carcinoma
  - Anal cancer
Over the past 2 decades, the incidence in Non-AIDS defining cancers is:

A. Increasing
B. Decreasing
C. Unchanged
Non-AIDS defining cancer

• Increasing incidence in the contemporary ART era
  – 4-fold cancer incidence increase from 1991 – 2005 (96,179 – 413,080 cases)
  – Now the leading cause of death among ART-experienced

  – AIDS-defining cancers decreased during same period

Non-AIDS defining cancer

• Role of immunosuppression
  – Both the HIV-infected population and solid organ transplant population are disproportionately affected by most cancer types
  • Immune deficiency is likely a strong contributor of oncogenesis in HIV overall

Non-AIDS defining cancer

- Duration of CD4 <200 cells/uL associated with higher risk of malignancy

1.12/year [95% CI, 1.03–1.22]

Non-AIDS defining cancer

- Higher risk of malignancy based on depth of recent CD4 count

![Graph showing event rate per 1000 PYFU vs. latest CD4 count (cells/µl)]

- CD4 <50: 6.0 (95% CI 3.3, 10.1)
- CD4 >500: 0.6 (95% CI 0.4, 0.8)

Non-AIDS defining cancer

• Other potential contributors:
  – Chronic immune activation/inflammation of HIV infection
  – Aging HIV-infected population
  – Higher smoking and EtOH-abuse prevalence of HIV-infected population
  – Co-infections with other viruses
Hodgkin Lymphoma
Hodgkin Lymphoma

• Risk in HIV infection is 10-25x higher than among general population
• HL tends to have more high-risk characteristics in HIV
• HIV-infected patients have more:
  – B Symptoms
  – Extra-nodal disease
  – Bone marrow involvement


Hodgkin Lymphoma

• High-risk features
  – Mixed cellularity histological subtype
  – Epstein-Barr virus (EBV) infection of the tumor cells
  – Advanced stage
  – Higher International Prognostic Score (IPS)

Hodgkin Lymphoma

• Outcomes are poorer
  – Predictive factors:
    • >45 years of age*
    • Male gender
    • Stage IV disease
    • Low albumin
    • Anemia
    • Lymphopenia
    • Leukocytosis

*Age >45 has been found to be significantly associated with progression or death (RR 8.1)!

Which age group is at highest risk for Hodgkin Lymphoma among the HIV+ population?

A. 20-25
B. 25-35
C. 35-45
D. 45-55
E. >55
Hodgkin Lymphoma

Hodgkin Lymphoma is most likely to occur at which CD4 count?

A. <50 cells/µL
B. 50 cells/µL
C. 100 cells/µL
D. 200 cells/µL
E. >200 cells/µL
Hodgkin Lymphoma

• Most cases occur at relatively high CD4 counts (>200 cells/µL)
  – Fast gain in CD4 T-cells after starting ART is associated with development of HL
  – Possible that CD4 T-cells support development of Reed-Sternberg cells
  – Immune reconstitution may contribute to the development of HL

• 80-100% associated with EBV (higher than in non-HIV HL)


Hodgkin Lymphoma

- HIV-associated HL tends to be unfavorable histological subtypes
  - Nodular sclerosis - 30% (HIV+) vs. 60% (HIV-)
  - Mixed cellularity - 25% (HIV+) vs. 12% (HIV-)
  - Lymphocyte deplete – 4% (HIV+) vs. 1% (HIV-)

Hodgkin Lymphoma

• Treatment
  – ABVD is standard therapy
  – ART can and should be used concurrently
    • Avoid PIs due to CYP450 3A4 interactions
    • Ritonavir can exacerbate vinblastine-induced neurotoxicity and neutropenia
  – Despite higher prevalence of high-risk features in HIV infection, prognosis is now on par with that of the general population.
    • ART is crucial

Hepatocellular carcinoma
Hepatocellular carcinoma

• Usually secondary to HBV or HCV co-infection
• Process is accelerated by HIV (increases HCC risk 7-fold)
  – Time to develop HCC after HCV infection is about 10 years shorter in setting of HIV
  – HIV increases risk of development of chronic HCV
  – HIV increases rate of fibrosis


Hepatocellular carcinoma

• Incidence varies by country
  – Highest in HBV endemic countries of East Asia, Africa
  – In developed countries, most are in HIV/HCV co-infection
    • Up to 25% of HIV+ patients have chronic HCV
    • 5-10% of HIV+ patients have chronic HBV


Hepatocellular carcinoma

• Usually asymptomatic initially
• Clinical presentation varies significantly depending on tumor growth rate, burden, number and location
Hepatocellular carcinoma

• HCC in HIV infection:
  – More advanced/infiltrative at diagnosis
  – More advanced cirrhosis at diagnosis
  – Younger age at diagnosis
  – Higher alpha-fetoprotein levels
  – Worse survival
    • Though not significantly worse if early stage
Hepatocellular carcinoma

• Curative treatment
  – Surgical resection
  – Radiofrequency ablation
  – Ethanol injection
  – Orthotopic liver transplantation

• Palliative treatment
  – Transarterial chemoembolization (TACE)
  – Kinase inhibitors
    • Sorafenib
    • Sutinib
    • Erlotinib
  – Systemic chemotherapy
Hepatocellular carcinoma

• Primary prevention
  – HBV vaccination
  – HCV screening and treatment
  – IVDU counseling
  – EtOH avoidance
  – Screening in cirrhotic patients
Lung cancer
Lung cancer

• Higher incidence among HIV+ adults (about 2-fold) than HIV- adults in USA

• Significant associations include older age, smoking >10 years, h/o Pneumocystis or recurrent pneumonia, h/o asthma

Lung cancer

• HIV+ with lung cancer
  – Tend to be younger
  – Present with more advanced disease
  – Have worse overall survival
  – May receive treatment less frequently
    • HIV+ adults found to be less likely to receive potentially curative resection
    • Less likely to receive chemotherapy, radiation
Lung cancer

• Survival

Head and Neck Squamous Cell Carcinoma
Head and Neck Squamous Cell Carcinoma

• Higher incidence of head and neck cancer (2 – 4-fold) in HIV infection

• HIV+ population has a higher prevalence of primary risk factors
  • Tobacco use
  • EtOH use
  • Oral HPV infection (2-fold higher)
  • More sexual partners

Head and Neck Squamous Cell Carcinoma

• 2 – 4-fold higher in HIV infection than among general population
  – Much more modest increased risk in HIV infection than among other HPV-associated cancers
  – Extent of HPV association in HIV infection is not well-characterized
  – Other factors are likely contributing
    • Immunosuppression
    • Tobacco use
Head and Neck Squamous Cell Carcinoma

- HIV+ adults with head and neck cancer:
  - Are mostly men, 91% (vs 68% among HIV-)
  - Are younger, median age 50 years (vs 62 years)
  - Are mostly nonwhite, 49% (vs 18%)
  - Are mostly current smokers, 61% (vs 18%)
  - Present at advanced stage, 60% (vs 20%)

Head and Neck Squamous Cell Carcinoma

• Poor survival outcome associations:
  – Current smoking (in both HIV+ and HIV-)
  – Lower CD4 count at diagnosis

• Poor prognosis associated with immunosuppression

Anal Cancer

• HPV-associated
• Incidence has not decreased in the contemporary ART era, likely increasing
• Highest risk population: HIV+ MSM, risk up to 128/100,000 (vs ~1.5-2/100,000 in the general population)
• The quadrivalent HPV vaccine has been shown to reduce anal HPV infection and neoplasia in men
Anal Cancer

• There are no national recommendations for routine anal cancer screening, but should be strongly considered in HIV-infected MSM and women (especially if history of other HPV-related lesions)

• Anal cancer screening should NOT be performed without the availability of high-resolution anoscopy (HRA)

https://aidsinfo.nih.gov/guidelines, accessed 7/7/17
Anal cancer

• Appropriate screening would include both cytology, HPV cotesting and DRE
• Abnormal cytology (ASCUS and LSIL), should get high-resolution anoscopy
• Any palpable masses on DRE or HSIL – referral to colorectal surgery
• Consider annual screening after normal cytology
High Resolution Anoscopy
Conclusions

• HIV-infected adults are at disproportionately high risk of many cancer types

• Contributing factors include immunosuppression, chronic inflammation, co-infections, and behaviors/exposures

• Outcomes are generally worse for HIV-infected patients

• Cancer prevention is a cornerstone of HIV care
  – Especially among those at high risk (i.e. chronic HCV)
Thank you!